REMARKS

Claims 1, 3-14 and 18-31 are currently pending in this application. Claim 18 has been amended. Claims 2 and 15-17 were previously cancelled without prejudice to or disclaimer of the subject matter contained therein. Claims 22-31 have been newly added.

Claim 18 has been amended to be in accordance with claim 1 in the active ingredients of the pharmaceutical formulation. Claims 22-31 are newly added to specify each of the two active ingredients in the pharmaceutical composition as recited in claim 1 and claim 18.

Support for the amendment to claim 18 and addition of claims 22-31 can be found throughout the specification and the claims as originally filed.

No new matter has been introduced to the claims within the meaning of 35 U.S.C. §132. Accordingly, entry of the amendments is respectfully requested.

I. Rejection of Claims 1, 3-14, 18 and 20-21 under 35 U.S.C. §103(a)

The Official Action states that claims 1, 3-14, 18 and 20-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Magee et al. (US Application Publication 2002/0111495).

As the basis of the rejection, the Official Action states in relevant part:

> Magee et al. teaches the use of selective PDE4 inhibitors for improved therapeutic treatment of a number of inflammatory, respiratory and allergic diseases including chronic rhinitis (para. 0467-0472). Magee et al. further teaches that the present compounds can be used together in combination with one or more therapeutic agents including antihistaminic H2 receptor antagonists such as azelastine, the steroid ciclesonide and with pharmaceutically [sic] carriers (cl.1, para. 0218 and 0570-0571).
>
> Magee et al. does not particularly teach a composition with a particular osmotic pressure or a composition containing microcrystalline cellulose as solid particles in an aqueous medium. However, Magee et al. does teach the inclusion of water-low soluble substance such as cellulose derivatives which encompasses all substances containing cellulose including microcrystalline

> cellulose [(MCC)] which are solid particles before addition to the pharmaceutical composition. Moreover, Magee et al. teaches the use of viscosity modifiers and given that [MCC] is a well-known viscosity modifier, one of ordinary skill would readily add such compound as solid particles as to obtain the desired product with the desired osmotic pressure. Additionally, Magee et al. teaches the addition of osmotic pressure controlling agents including glucose and sodium chloride. Consequently, these agents would necessarily affect the osmotic pressure of the composition due to their isotonization properties. Thus, to acquire the desired osmotic pressure for enhancing the bioavailability of the active ingredients as suggested by Magee et al., one of ordinary skill would be motivated to vary the concentration of the osmotic pressure controlling agents in a particular form of the composition. Moreover, applicant is reminded that a prior art reference may "render obvious" without disclosing a feature of the claimed invention, as long as that missing characteristic is necessarily present, or inherent, in the anticipation reference. ... In the instant case, the unappreciated osmotic pressure of Magee's composition does not require recognition by Magee et al.

Applicants respectfully traverse this rejection. The cited reference does not establish a *prima facie* case of obviousness against the presently pending claims. Any alleged *prima facie* case of obviousness is also rebutted by the unexpected results of the present claims.

To establish a *prima facie* case of obviousness, the PTO must satisfy three requirements. First, as the U.S. Supreme Court held in *KSR International Co. v. Teleflex Inc. et al.*, 550 U.S. 398 (2007), "a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions. ...it [may] be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. ...it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does... because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will

be combinations of what, in some sense, is already known." *See KSR International Co. v. Teleflex Inc. et al.*, 550 U.S. 398 at 417-418. Second, the proposed modification of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. *Amgen Inc. v. Chugai Pharm. Co.*, 18 USPQ2d 1016, 1023 (Fed. Cir. 1991). Lastly, the prior art references must teach or suggest all the limitations of the claims. *In re Wilson*, 165 USPQ 494, 496 (C.C.P.A. 1970).

Further, a *prima facie* case of obviousness, if established, can be rebutted when the claimed invention yields unexpectedly improved properties or properties not present in the prior art. Rebuttal evidence may consist of a showing that the claimed compound possesses unexpected properties. *In re Dillon*, 919 F.2d at 692-93, 16 USPQ2d at 1901. When considering whether proffered evidence is commensurate in scope with the claimed invention, office personnel should not require the applicants to show unexpected results over the entire range of properties possessed by a chemical compound or composition. *In re Chupp*, 816 F.2d 643, 646, 2 USPQ2d 1437, 1439 (Fed. Cir. 1987). Evidence that the compound or composition possesses superior and unexpected properties in one of a spectrum of common properties can be sufficient to rebut a *prima facie* case of obviousness. *Id.*

Present Subject Matter

The present subject matter relates to a pharmaceutical composition for application to the mucosa comprising, as active ingredients, a combination of 4-[(4-chlorophenyl)methyl]-2-(hexahydro-1-methyl-1H-azepin-4-yl)-1(2H)phthalazinone (AZELASTINE), or a stereoisomer, a pharmaceutically acceptable salt or physiologically functional derivative thereof, and ciclesonide, or a pharmaceutically acceptable salt of ciclesonide, an epimer of

ciclesonide, or a physiologically functional derivative of ciclesonide, and a pharmaceutically acceptable carrier and/or one or more excipients (hereinafter, "a combination of azelastine and ciclesonide"), wherein said pharmaceutical composition has an osmotic pressure of less than 290 mOsm, as described in the broadest claim 1, and to a method for the treatment of allergic rhinitis and/or allergic conjunctivitis in a mammal by administrating to a mammal said pharmaceutical composition, as described by claim 18.

Applicants submit that it has been surprisingly found in the present application that combined administration of a combination of ciclesonide and azelastine, as described at paragraphs [0013] and [0038] of the published present specification (US Pub. No. 2005-0245493), results in a very effective and safe treatment of symptoms accompanied with allergic rhinitis and/or allergic conjunctivitis. That is, by the combined administration of the two specific active ingredients, as a "hypotonic" aqueous pharmaceutical formulation, a "rapid onset of action and quick symptom relief" was observed without the disadvantage of glucocorticoid like side effects. Therefore, in the presently claimed composition, "very low doses" of ciclesonide are present, yet only a once-daily, or maximum twice-daily treatment is required to achieve an effective treatment.

The other presently rejected claims 3-14, 18 and 20-21 are, directly or indirectly, dependent from claim 1 or claim 18, and thus incorporate all of the limitations of claim 1 or claim 18 as noted above. If an independent claim is nonobvious under 35 U.S.C. §103, then any claim depending therefrom is likewise nonobvious. *In re Fine,* 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988).

Magee et al. do not establish a prima facie case of obviousness against the present subject matter.

The teachings of Magee et al. are discussed in our previous responses filed on

September 23, 2008 and July 22, 2009. For the sake of brevity, the discussions therein are incorporated herein by reference in their entirety.

Accordingly, Magee et al. fail to disclose, teach or suggest, expressly or inherently, a "hypotonic" composition, as required by present claim 1, i.e., the limitation of "less than 290 mOsm." As discussed, Magee et al. teach an isotonic (290 mOsm) composition, teaching away from the claimed hypotonic composition. *See* paragraph [0708] of Magee et al.

Further, Magee et al. fail to teach "a combination of azelastine and ciclesonide" as an active ingredient of the nasal composition. The "laundry list" of over several hundreds of potential active ingredients, described at paragraph [0218] of Magee et al., does not teach at all a specific composition having a combination of the two specific active ingredients as an active ingredient. The nearly one page long paragraph teaches nothing but a general possibility of the combined use a PDE4 inhibitor - the active ingredient of the compositions disclosed therein - with one or more of the listed components. Without further disclosure regarding the benefits obtainable from the combination of the two specific active ingredients, i.e., azelastine and ciclesonide, there is absolutely no reason for a person of ordinary skill to choose and combine the presently claimed two specific ingredients from the disclosed lengthy list. Likewise, a person of ordinary skill would have had no reason to modify the Magee et al. compositions containing the two active ingredients to achieve a "hypotonic" composition. The teaching of an "isotonic" composition in Magee et al. would have directed a person of ordinary skill away from this modification toward a hypotonic composition, as required by the present claims.

As such, Magee et al. clearly fail to teach all of the limitations of the present claims, as required by *In re Wilson*. Further, a person of ordinary skill in the art would have had no apparent reason to choose and combine the two specific ingredients in the same way

required by the present claims, as required by *KSR International Co. v. Teleflex Inc. et al.*

Accordingly, a *prima facie* case of obviousness has not been established in the present application against presently pending claims 1, 3-14, 18 and 20-21. Reconsideration and withdrawal of this rejection is therefore respectfully requested.

Any alleged prima facie case of obviousness is rebutted by the unexpected results of the present claims – CFR §1.132 Declaration by Dr. Rolf Beume.

Applicants additionally submit that the presently claimed subject matter shows unexpected results and advantages that are not presented in the prior art, which rebuts any alleged *prima facie* case of obviousness. *In re Dillon,* 919 F.2d at 692-93, 16 USPQ2d at 1901. Rebuttal evidence may include evidence that the claimed subject matter yields unexpectedly improved properties or properties not present in the prior art. Rebuttal evidence may consist of a showing that the claimed compound possesses unexpected properties. *See In re Dillon.* Further, rebuttal evidence and arguments can be presented in the specification, *In re Soni*, 54 F.3d 746, 750, 34 USPQ2d 1684, 1687 (Fed. Cir. 1995), by counsel, *In re Chu*, 66 F.3d 292, 299, 36 USPQ2d 1089, 1094-95 (Fed. Cir. 1995), or by way of an affidavit or declaration under 37 CFR 1.132, e.g., *Soni*, 54 F.3d at 750, 34 USPQ2d at 1687; *In re Piasecki*, 745 F.2d 1468, 1474, 223 USPQ 785, 789-90 (Fed. Cir. 1984).

In this regard, Applicants direct the Examiner's attention to the description at paragraph [038] of the published present application, as below:

> "Due to the unique galenic formulation, ciclesonide rapidly enters the nasal mucosa and has a very long retention time. Therefore, very low doses of ciclesonide and the once daily, maximal twice-daily treatment is necessary to achieve an effective treatment. A low dose of ciclesonide in a hypotonic watery suspension in combination with a topical antihistamine (e.g. azelastine or levocabastine) results in a very effective and safe treatment of all symptoms accompanied with allergic rhinitis. A clear advantage of this combination is the

rapid onset of action and quick symptom relief without the fear of glucocorticoid like side effects." [Emphasis added]

These beneficial effects of a rapid onset of action and quick symptom relief provided by the present subject matter are not presented in any prior art of record, including Magee et al.

Also, the unexpected results of the present subject matter are supported by the experimental data presented in the Declaration by Dr. Rolf Beume submitted herewith under 37 CFR §1.132.

As confirmed by the results in Figures 1 and 2 attached to the Declaration, the number of sneezes/mouse during the first 10 minutes after challenge (compound score challenge 1-3) was significantly increased in the allergic control group. While the combination treatment of ciclesonide and azelastine showed a significant reduction in sneezes (Fig. 1), azelastine and ciclesonide alone had little or no effects, respectively. Also, during the first 10 minutes after the first challenge, the number of nasal rubbings/mouse was significantly increased in the allergic control group. All treatment groups displayed a significant reduction in the number of rubbings/mouse with the combination of ciclesonide and azelastine displaying a superior effect (Fig. 2).

Accordingly, the data presented in the Declaration provides clear evidence that the presently claimed subject matter shows unexpectedly superior results of the rapid onset and quick symptom relief, as compared to the either agent alone. That is, it is clear from the data that the presently claimed combination of ciclesonide and azelastine is unexpectedly superior in reducing the occurrence of sneezes and nasal rubbings. The combination product yielded a much greater than additive effect when compared to each of the separate agents by themselves.

As such, Applicants submit that any alleged *prima facie* case of obviousness is rebutted by the unexpected results of the presently claimed subject matter as shown in the Declaration. *See In re Dillon*.

The Examiner is respectfully requested to reconsider and withdraw the rejection of claims 1, 3-14 and 18-21 under 35 U.S.C. § 103(a).

III. Rejection of Claim 19 under 35 U.S.C. §103(a)

The Official Action states that claim 19 is rejected under 35 U.S.C. 103(a) as being obvious over Magee et al. (US Application Publication 2002/0111495) in view of Calatayud et al. (US Patent No. 5,482,934)

As the basis of the rejection, the Official Action states in relevant part:

> ... one of ordinary skill in the art at the time of the invention would have found it obvious to substitute the mixture of epimers of ciclesonide into the composition of Magee et al. to treat allergic rhinitis while varying the concentration of the osmotic pressure controlling agents since Calatayud et al. tech that the mixture of epimers possesses intense glucocorticoid and therapeutic activities with minimal systemic effects. Given that Magee et al. teach a method of treating allergic rhinitis with PDE4 inhibitors, azelastine and ciclesonide with additional exipients, and Calatayud et al. teach mixtures of epimers of ciclesonide with high glucocorticoid activity and minimal systemic effects, one of ordinary skill would have been motivated to substitute the mixture of epimers of ciclesonide into the composition of Magee et al. with the reasonable expectation of providing a composition that is efficacious in treating allergic rhinitis and a composition that is readily absorbed with no systemic effects.

Applicants respectfully traverse this rejection. The cited references do not establish a *prima facie* case of obviousness against the presently pending claims. In addition, any alleged *prima facie* case of obviousness is rebutted by the unexpected results of the present claims.

Claim 19 is directed to "The pharmaceutical composition according to claim 1, wherein said epimer of ciclesonide is [11β,16α(S)]-16,17-[(cyclohexylmethylen)bis(oxy)]-11-

hydroxy-21-(2-methyl-1-oxopropoxy)-pregna-1,4-dien-3,20-dion and is present in any mixing ratio with ciclesonide, [11β,16α(R)]-16,17-[(cyclohexylmethylen)bis(oxy)]-11-hydroxy-21-(2-methyl-1-oxopropoxy)-pregna-1,4-dien-3,20-dion." Accordingly, claim 19 incorporate all of the limitations of present claim 1. The discussion of present claim 1 and Applicants' arguments regarding the teachings of the Magee et al. reference outlined at pages 11-13 of this paper are incorporated herein in their entirety. Accordingly, Magee et al. fail to teach or suggest all of the limitations of the present claims, as required by *In re Wilson*. Also, there is absolutely no reason for a person of ordinary skill in the art to choose and combine the presently claimed two specific ingredients from the lengthy list disclosed in Magee et al., as required by *KSR International Co. v. Teleflex Inc. et al.*

Calatayud et al. cannot remedy the deficiencies of Magee et al.

Calatayud et al. has been cited by the Examiner to cure the deficient teaching of Magee et al. regarding the limitation of claim 19, i.e., the teaching of R and S epimers of ciclesonide in a certain mixing ratio. However, assuming *arguendo* that Calatayud et al. teach the mixture of R and S epimers of ciclesonide, the reference does not teach any particular osmotic pressure, much less the hypotonic compositions of the presently pending claims. Further, Calatayud et al. do not teach a combination of ciclesonide and azelastine, as an active ingredient for a nasal composition.

Accordingly, even with the combination of Magee et al. and Calatayud et al., the Examiner has failed to establish a *prima facie* case of obviousness against the presently pending claims because both the references fail to teach all of the limitations of the presently pending claims as required by *In re Wilson*. Reconsideration and withdrawal of this rejection is therefore respectfully requested.

Any alleged prima facie case of obviousness is rebutted by unexpected results of the present claims – CFR §1.132 Declaration by Dr. Rolf Beume.

If the Examiner insists that a *prima facie* case of obviousness has been established, Applicants submit that any alleged *prima facie* case of obviousness is rebutted by the unexpected results of the present claims as supported by the description of the present specification and the experimental data in the Declaration by Dr. Rolf Beume. The discussion of the experimental data and the unexpected results of the present claims presented at pages 13-15 of this paper is incorporated herein in its entirety. As discussed, the presently claimed subject matter shows unexpectedly superior results of the rapid onset and quick symptom relief, as compared to the either agent alone, which rebuts any alleged *prima facie* case of obviousness against the presently claimed subject matter as held by the *In re Dillon* court.

As such, the Examiner is respectfully requested to withdraw this rejection of presently pending claim 19.

III. Rejection of Claims 1, 3-14, 18 and 20-21 under 35 U.S.C. §103(a)

The Official Action states that claims 1, 3-14, 18 and 20-21 are rejected under 35 U.S.C. 103(a) as being obvious over Szelenyl et al. (WO01/22955-corresponding to US Patent No. 7,022,687) in view of Schmidt et al. (J. Clin. Pharmacol. 1999, Vol. 39, pp. 1062-1069).

As the basis of the rejection, the Official Action states in relevant part:

> ... one of ordinary skill in the art at the time of the invention would have found it obvious to substitute the ciclesonide of Schmidt et al. for the loteprednol of Szelenyl et al. to treat allergic rhinitis since Schmidt et al. teach that ciclesonide possesses low systemic effects. Moreover, as a general principle it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose, the idea of combining them

> flows logically from their having been individually taught in the prior art. ... Given that Szelenyl et al. teach a composition containing a soft steroid and antihistamines for treating allergic rhinitis with additional excipients, and Schmidt et al. teach the soft steroid ciclesonide is effective in treating allergic rhinitis without producing local or systemic effects, one of ordinary skill would have been motivated to substitute the ciclesonide of Schmidt et al. for the loteprednol of Szelenyl et al. with the reasonable expectation of providing a composition that is efficacious in treating allergic rhinitis and a composition with minimal side effects.

Applicants respectfully traverse this rejection. Again, the cited references do not establish a *prima facie* case of obviousness against the presently pending claims. In addition, any alleged *prima facie* case of obviousness is rebutted by the unexpected results of the presently claimed subject matter.

The present subject matter is discussed at pages 11 and 12 of this paper and is incorporated herein in its entirety. As discussed, in the presently claimed composition, the combined administration of the two specific active ingredients as a "hypotonic" aqueous pharmaceutical nasal composition results in the "rapid onset of action" and "quick symptom relief" without the fear of glucocorticoid like side effects. Therefore, "very low doses" of ciclesonide are present, yet only a once-daily, or maximum twice-daily treatment is required to achieve an effective treatment by the present composition.

Szelenyl et al. and Schmidt et al. fail to teach all of the limitations of the present claims - a failure to establish prima facie case of obviousness.

Szelenyl et al. describe a combination of a soft steroid, particularly loteprednol, and at least one antihistamine, such as azelastine and/or levocabastine, for simultaneous, sequential or separate administration in the local treatment of allergies and airway disorders, for example of allergic rhinitis. Szelenyl et al. further describe the use of excipients for the adjustment of the isotonicity of the formulations disclosed therein.

However, like Magee et al., Szelenyl et al. do not teach or suggest a combination of

ciclesonide and azelastine, nor a hypotonic composition, as required by the present claims. Applicants draw the Examiner's attention to the description at col. 4, lines 29-33 of the corresponding '687 US Patent to Szelenyl et al. This section of the reference discusses suitable excipients for making the formulations isotonic. As with Magee et al., Szelenyl et al. teach the ordinary skilled artisan away from making the presently claimed hypotonic formulations.

Schmidt et al. do not remedy the deficient teachings of Szelenyl et al. Schmidt et al. describe that a topical steroid, ciclesonide, is effective in the treatment of allergic rhinitis. However, Schmidt et al. do not teach any particular osmotic pressure, much less the hypotonic compositions of the present claims. Accordingly, Szelenyl et al. and Schmidt et al., taken alone or together, fail to teach all of the limitations of the present claims as required by *In re Wilson*.

Accordingly, Applicants submit that a *prima facie* case of obviousness against the presently pending claims has not been established. Reconsideration and withdrawal of this rejection is therefore respectfully requested.

Any alleged prima facie case of obviousness is rebutted by unexpected results of the present claims – CFR §1.132 Declaration by Dr. Rolf Beume.

Applicants additionally submit that the presently claimed subject matter shows unexpected results and advantages that are not presented in the prior art of record, including Szelenyl et al. and Schmidt ea al., which rebuts any alleged *prima facie* case of obviousness. *In re Dillon,* 919 F.2d at 692-93, 16 USPQ2d at 1901. Rebuttal evidence may include evidence that the claimed subject matter yields unexpectedly improved properties or properties not present in the prior art. Rebuttal evidence may consist of a showing that the claimed compound possesses unexpected properties. *See In re Dillon*. Further, rebuttal

evidence and arguments can be presented in the specification, *In re Soni*, 54 F.3d 746, 750, 34 USPQ2d 1684, 1687 (Fed. Cir. 1995), by counsel, *In re Chu*, 66 F.3d 292, 299, 36 USPQ2d 1089, 1094-95 (Fed. Cir. 1995), or by way of an affidavit or declaration under 37 CFR 1.132, e.g., *Soni*, 54 F.3d at 750, 34 USPQ2d at 1687; *In re Piasecki*, 745 F.2d 1468, 1474, 223 USPQ 785, 789-90 (Fed. Cir. 1984).

The unexpected results of the present claims are supported by the description in the originally filed specification and the experimental data in the Declaration by Dr. Rolf Beume submitted herewith. The discussion of the experimental data in the Declaration and the unexpected results of the present claims presented at pages 13-15 of this paper is incorporated herein in its entirety. As discussed, the presently claimed subject matter shows unexpectedly superior results of the rapid onset and quick symptom relief as compared to the either agent alone.

Accordingly, any alleged *prima facie* case of obviousness is rebutted by the unexpected results shown for the presently claimed composition. The Examiner is therefore respectfully requested to reconsider and withdraw this rejection of presently pending claim 1, 3-14, 18 and 20-21.

IV. Rejection of Claim 19 under 35 U.S.C. §103(a)

The Official Action states that claim 19 is rejected under 35 U.S.C. 103(a) as being obvious over Szelenyl et al. in view of Schmidt et al. and further in view of Calatayud et al.

As the basis of the rejection, the Official Action states in relevant part:

> ... one of ordinary skill in the art at the time of the invention would have found it obvious to substitute the mixture of epimers of ciclesonide into the composition of Szelenyl et al. to treat allergic rhinitis since Calatayud et al. teach that the mixture of epimers possesses intense glucocorticoid and therapeutic activities with minimal systemic effects. Given that Szelenyl et al. teach a composition of treating allergic rhinitis with azelastine and levocabastine and a soft steroid

along with additional excipients, and Schmidt et al teach the use of ciclesonide for treating allergic rhinitis with high glucocorticoid activity and minimal systemic effects, one of ordinary skill would have been motivated to substitute the mixture of epimers of ciclesonide into the composition of Szelenyl et al. with the reasonable expectation of providing a composition that is efficacious in treating allergic rhinitis and a composition that is readily absorbed with no systemic effects.

Applicants respectfully traverse this rejection. Again, the cited references do not establish a *prima facie* case of obviousness against the presently pending claims and any alleged *prima facie* case of obviousness is rebutted by the unexpected results of the present claims.

Claim 19 is directed to "The pharmaceutical composition according to claim 1, wherein said epimer of ciclesonide is [11β,16α(S)]-16,17-[(cyclohexylmethylen)bis(oxy)]-11-hydroxy-21-(2-methyl-1-oxopropoxy)-pregna-1,4-dien-3,20-dion and is present in any mixing ratio with ciclesonide, [11β,16α(R)]-16,17-[(cyclohexylmethylen)bis(oxy)]-11-hydroxy-21-(2-methyl-1-oxopropoxy)-pregna-1,4-dien-3,20-dion." Accordingly, claim 19 incorporate all of the limitations of present claim 1. The discussion of claim 1 and Applicants' arguments regarding the teachings of Szelenyl et al. and Schmidt et al. outlined at pages 19 and 20 of this paper are incorporated herein by reference in their entirety. Accordingly, neither Szelenyl et al., nor Schmidt et al. disclose, teach or suggest all of the limitations of present claim 1, as required by *In re Wilson*.

Calatayud et al. do not remedy the deficiencies of Szelenyl et al. or Schmidt et al.

Calatayud et al. has been cited by the Examiner to cure the deficient teaching of Szelenyl et al. and Schmidt et al. regarding the limitation of claim 19, namely no teaching of R and S epimers of ciclesonide in a certain mixing ratio.

However, Calatayud et al. do not teach any particular osmotic pressure, much less

the hypotonic compositions of the presently pending claims. Further, Calatayud et al. do not teach a combination of ciclesonide and azelastine, as an active ingredient for a nasal composition.

Accordingly, even in combination with Calatayud et al., both the references of Szelenyl et al. and Schmidt et al. do not establish a *prima facie* case of obviousness against the presently pending claims because none of the three cited references teach or suggest all of the limitations of the presently pending claims, as required by *In re Wilson*.

Any alleged prima facie case of obviousness is rebutted by unexpected results of the present claims – CFR §1.132 Declaration by Dr. Rolf Beume.

If the Examiner insists that a *prima facie* case of obviousness has been established, Applicants submit that any alleged prima facie case of obviousness is rebutted by the unexpected results of the present claims as supported by the description in the present specification and the experimental data in the Declaration by Dr. Rolf Beume. For the sake of brevity, all of the discussion regarding the experimental data and the unexpected results of the present claims, presented at pages 13-15 of this paper, is incorporated herein in its entirety. Accordingly, the presently claimed subject matter shows unexpectedly superior results of rapid onset and quick symptom relief, as compared to the either agent alone. Any alleged *prima facie* case of obviousness is therefore rebutted by the unexpected results of the presently claimed subject matter. *See In re Dillon*.

As such, the Examiner is respectfully requested to reconsider and withdraw this rejection of presently pending claim 19.

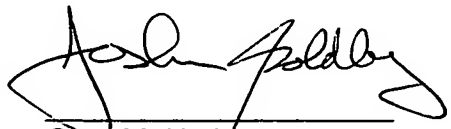
CONCLUSION

Based upon the remarks, the presently claimed subject matter is believed to be patentably distinguishable over the prior art of record. The Examiner is therefore respectfully requested to reconsider and withdraw the outstanding rejections and allow all pending claims 1, 3-14 and 18-31. Favorable action with an early allowance of the claims pending in this application is earnestly solicited.

The Examiner is welcomed to telephone the undersigned attorney if he has any questions or comments. The Examiner is specifically authorized to charge any fee deficiency or credit any overpayment to Deposit Account No. 14-0112.

Respectfully submitted,

THE NATH LAW GROUP



Gary M. Nath
Reg. No. 26,965
Joshua B. Goldberg
Reg. No. 44,126
Customer No. 34375

Date: February 26, 2010

THE NATH LAW GROUP
112 S. West Street
Alexandria, VA 22314
Tel: (703) 548-6284
Fax: (703) 683-8396

JBG/MSK/ROA4